

08/307621

"=> s transglutaminase"  
"L1 107 TRANSGLUTAMINASE"  
"=> s collagen"  
"L2 8200 COLLAGEN"  
"=> s l1 and l2"  
"L3 38 L1 AND L2"  
"=> d l3 1-38"  
" "  
"1. 5",514,579," May 7"," 1996"," Human transglutaminases;  
Patrick J. O'Hara",""  
"et al.", " 435/240.2", " 69.2", " 193", " 254.3", " 320.1;  
536/23.2", " 24.31 [IMAGE"  
"AVAILABLE] "  
" "  
"2. 5",510,102," Apr. 23"," 1996"," Plasma and polymer  
containing surgical"  
"hemostatic adhesives; Kent C. Cochrum", " 424/78.08; 128/DIG.22;  
424/530;"  
"602/52 [IMAGE AVAILABLE] "  
" "  
"3. 5",510,077," Apr. 23"," 1996"," Method of making an  
intraluminal stent;"  
"Thomas Q. Dinh", " et al.", " 264/485", " 279", " 279.1", " 314", "  
316", " 320", " 330", " 488"  
"[IMAGE AVAILABLE] "  
" "  
"4. 5",504,001," Apr. 2"," 1996"," Hybrid plasminogen activator;  
Donald C."  
"Foster", " 435/219; 424/94.64; 435/226 [IMAGE AVAILABLE] "  
" "  
"5. 5",490,980," Feb. 13"," 1996"," Covalent bonding of active  
agents to skin",""  
"hair or nails; Norman K. Richardson", " et al.", " 424/94.6; 514/2  
[IMAGE"  
"AVAILABLE] "  
" "  
"6. 5",487,889," Jan. 30"," 1996"," Bandage for continuous  
application of"  
"biologicals; Richard L. Eckert", " et al.", " 424/93.1", " 93.2", "  
93.21", " 93.7;"  
"514/2", " 12; 604/304", " 305", " 307 [IMAGE AVAILABLE] "  
" "  
"7. 5",486,599," Jan. 23"," 1996"," Construction and use of  
synthetic"  
"constructs encoding syndecan; Scott Saunders", " et al.", "  
530/395; 435/69.1", "  
"69.7", " 252.3", " 320.1; 536/23.4", " 23.5; 935/10", " 47", " 50", "  
70 [IMAGE AVAILABLE] "  
" "  
"8. 5",475,113," Dec. 12"," 1995"," Tetrahydronaphthyl and  
thiazole", " oxazole or"  
"imidazole substituted ethene derivatives having retinoid-like  
activity", "  
"reduced skin toxicity and reduced teratogenecity; Roshantha A."

"Chandraratna", " 548/203", " 200", " 204", " 205", " 214", " 235", " 236", " 333.5", " 334.5 [IMAGE"

"AVAILABLE]"

" "

"9. 5", 455, 265, " Oct. 3", " 1995", " Method of treatment with compounds having"

"selective agonist-like activity on RXR retinoid receptors;

Roshantha A."

"S. Chandraratna", " 514/448", " 438", " 444", " 452", " 461", " 467", " 471", " 510", " 531", " 546", ""

569, " 617", " 684", " 700", " 717", " 719", " 729", " 765; 549/60", " 70", " 71", " 72", " 73", " 74", " 75", ""

77, " 78", " 79", " 80", " 369", " 370", " 430", " 448", " 468", " 483", " 486", " 487", " 493", " 495", " 496", ""

497, " 498", " 499", " 501", " 504", " 505", " 506; 560/8", " 100; 562/405", " 490; 564/180; "

"568/327", " 328", " 440", " 592", " 659", " 808; 585/20", " 21 [IMAGE

AVAILABLE]"

" "

"10. 5", 455, 158, " Oct. 3", " 1995", " Fibrin binding domain polypeptides and uses"

"and methods of producing same; Tikva Vogel", " et al.", " 435/7.21; 424/1.69", ""

"9.341", " 9.4; 435/7.8", " 13; 436/69", " 503", " 504 [IMAGE

AVAILABLE]"

" "

"11. 5", 428, 014, " Jun. 27", " 1995", " \*\*Transglutaminase\*\* cross-linkable"

"polypeptides and methods relating thereto; Virender Labroo", " et al.", ""

"514/12", " 13", " 14", " 15", " 16; 530/324", " 326", " 327", " 328", " 329", " 345", " 350 [IMAGE"

AVAILABLE]"

" "

"12. 5", 409, 731, " Apr. 25", " 1995", " Method for imparting a hydrophilic nature"

"to a contact lens; Akira Nakagawa", " et al.", " 427/2.12", " 164", " 338", " 340", " 393.5"

"[IMAGE AVAILABLE]"

" "

"13. 5", 368, 858, " Nov. 29", " 1994", " Methods and compositions for the treatment"

"and repair of defects or lesions in cartilage; Ernst B. Hunziker", ""

"424/423", " 424", " 425", " 426", " 450", " 484", " 489", " 499; 514/944", " 953", " 965 [IMAGE"

AVAILABLE]"

" "

"14. 5", 366, 958, " Nov. 22", " 1994", " Localized delivery using fibronectin"

"conjugates; Alan L. Weiner", " et al.", " 514/2; 424/450; 530/380", " 810", " 812"

"[IMAGE AVAILABLE]"

" "

"14. 5", 366, 958, " Nov. 22", " 1994", " Localized delivery using fibronectin"

"conjugates; Alan L. Weiner", " et al.", " 514/2; 424/450; 530/380", " 810", " 812"

"[IMAGE AVAILABLE]"

" "

"14. 5", 366, 958, " Nov. 22", " 1994", " Localized delivery using fibronectin"

"conjugates; Alan L. Weiner", " et al.", " 514/2; 424/450; 530/380", " 810", " 812"

"[IMAGE AVAILABLE]"

" "

"15. 5",324,840," Jun. 28"," 1994"," Method of treatment with compounds having"  
"retinoid-like activity and reduced skin toxicity and lacking teratogenic"  
"effects; Roshantha A. S. Chandraratna"," 546/318"," 326"," 335"," 342; 549/77",""  
79," 484"," 487"," 496"," 499 [IMAGE AVAILABLE] "  
" "

"16. 5",312,751," May 17"," 1994"," Hybridoma producing a monoclonal antibody"  
"specific for an antigen of the stratum corneum of human epidermis; Serge"  
"Michel"," et al."," 435/240.27"," 70.21"," 172.2; 530/388.2 [IMAGE AVAILABLE] "  
" "

"17. 5",271,961," Dec. 21"," 1993"," Method for producing protein microspheres;"  
"Edith Mathiowitz"," et al."," 427/213.31; 424/491"," 499; 426/96; 427/213.3",""  
"213.36 [IMAGE AVAILABLE] "  
" "

"18. 5",270,300," Dec. 14"," 1993"," Methods and compositions for the treatment"  
"and repair of defects or lesions in cartilage or bone; Ernst B. Hunziker",""  
"514/12; 424/422"," 423"," 424"," 425"," 426"," 450"," 484"," 489"," 499; 514/2"," 8"," 56",""  
944," 965; 530/350"," 351"," 353"," 354"," 356"," 840 [IMAGE AVAILABLE] "  
" "

"19. 5",270,030," Dec. 14"," 1993"," Fibrin binding domain polypeptide and"  
"method of producing; Tikva Vogel"," et al."," 424/1.69"," 9.341"," 9.4; 435/69.1",""  
"240.1"," 252.3"," 252.33"," 320.1; 530/350"," 395 [IMAGE AVAILABLE] "  
" "

"20. 5",206,023," Apr. 27"," 1993"," Method and compositions for the treatment"  
"and repair of defects or lesions in cartilage; Ernst B. Hunziker",""  
"424/423"," 422"," 424"," 425"," 426"," 450"," 484"," 489"," 499; 514/2"," 8"," 944"," 953"," 965;"  
"530/350"," 351"," 353"," 354"," 356"," 840 [IMAGE AVAILABLE] "  
" "

"21. 5",204,447," Apr. 20"," 1993"," Purification of factor XIII; Paul D."  
"Bishop"," et al."," 530/381"," 380"," 416"," 417"," 418"," 419"," 420"," 421 [IMAGE AVAILABLE] "  
" "

"22. 5",177,092," Jan. 5"," 1993"," Medicinal use of certain tetrazolium salts;"  
"David C. Remy"," et al."," 514/381; 548/251 [IMAGE AVAILABLE] "

" "

"23. 5",156,956," Oct. 20"," 1992"," Transgultaminase; Masao Motoki"," et al.",""  
 "435/68.1; 426/573; 435/193 [IMAGE AVAILABLE]"

" "

"24. 5",152,988," Oct. 6"," 1992"," Imidazole compounds in compositions and"  
 "methods in thrombolytic therapy; David A. Claremon"," et al.","  
 424/94.64;"  
 "514/2"," 14"," 161"," 213"," 228.2"," 255"," 257 [IMAGE AVAILABLE]"

" "

"25. 5",151,412," Sep. 29"," 1992"," Pharmaceutically active conjugates having"  
 "improved body tissue binding specificity; Robert A. Brown"," 514/8;"  
 "435/177; 514/2"," 6"," 21; 530/363"," 380"," 382"," 391.9"," 395"," 400"," 402 [IMAGE AVAILABLE]"

" "

"26. 5",098,733," Mar. 24"," 1992"," Novel gel-like food articles and process"  
 "for producing the same; Nobuo Kyogoku"," et al.", " 426/573"," 104"," 574"," 656;"  
 "530/378"," 408 [IMAGE AVAILABLE]"

" "

"27. 5",098,707," Mar. 24"," 1992"," Imidazole compounds and their use as"  
 "\*\*transglutaminase\*\* inhibitors; John J. Baldwin"," et al.", " 424/94.64;"  
 "514/2"," 56"," 161"," 258"," 398"," 822 [IMAGE AVAILABLE]"

" "

"28. 5",093,028," Mar. 3"," 1992"," Gelled emulsion and process for producing"  
 "the same; Nobuo Kyogoku"," et al.", " 252/315.1"," 312; 426/573 [IMAGE AVAILABLE]"

" "

"29. 5",084,444," Jan. 28"," 1992"," Imidazole compounds and their use as"  
 "\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.", " 514/15"," 16"," 18," 393; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"30. 5",077,285," Dec. 31"," 1991"," Imidazole compounds and their use as"  
 "\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.", " 514/15"," 16"," 18; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"31. 5",047,416," Sep. 10"," 1991"," Triazole compounds and their use as"  
 "\*\*transglutaminase\*\* inhibitors; David C. Remy"," et al.", " 514/384; 546/119;"

"548/251", " 255", " 264.4", " 370.4 [IMAGE AVAILABLE] "

" 32. 5", 037, 664, " Aug. 6", " 1991", " Process for producing novel gel-like food"

"articles; Nobuo Kyogoku", " et al.", " 426/573", " 656; 530/408 [IMAGE AVAILABLE] "

" 33. 5", 030, 644, " Jul. 9", " 1991", " Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; John J. Baldwin", " et al.", " 514/393", " 252", " "

253, " 256", " 278", " 338", " 341", " 395", " 398; 544/333", " 406; 546/15", " 271", " 278; "

"548/302.7", " 307.1", " 321.5", " 324.1 [IMAGE AVAILABLE] "

" 34. 5", 021, 440, " Jun. 4", " 1991", " Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; David C. Remy", " et al.", " 514/381", " 393", " "

"397; 548/251", " 302.7", " 312.7", " 324.1", " 325.1 [IMAGE AVAILABLE] "

" 35. 5", 019, 572, " May 28", " 1991", " Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; David A. Claremon", " et al.", " 514/213", " "

"228.2", " 255", " 326", " 398; 540/451; 544/61", " 359; 546/210; 548/302.7", " 314.7", " "

"315.1", " 315.7", " 324.1", " 325.1 [IMAGE AVAILABLE] "

" 36. 4", 968, 713, " Nov. 6", " 1990", " Certain imidazole compounds as"

"\*\*transglutaminase\*\* inhibitors; John J. Baldwin", " et al.", " 514/398; "

"548/324.1 [IMAGE AVAILABLE] "

" 37. 4", 407, 787, " Oct. 4", " 1983", " Collagenous dressing; Axel Stemberger", " "

"424/444; 106/122", " 125", " 128", " 161; 514/21", " 57", " 801", " 802; 530/356", " 381; "

"602/49", " 50; 604/304 [IMAGE AVAILABLE] "

" 38. 4", 325, 867, " Apr. 20", " 1982", " Process for the recovery of"

".alpha.-2-SB-glycoprotein; Walter Eberle", " et al.", " 530/392", " 353", " 354", " 356", " "

381, " 395", " 411", " 413", " 830 [IMAGE AVAILABLE] "

"=> d l3 37 kwic"

"US PAT NO: 4", 407, "787 [IMAGE AVAILABLE]  
of 38"

L3: 37

"ABSTRACT: "

"A collagenous dressing which is characterized in that it contains"  
 "\*\*collagen\*\* in combination with a resorbable biopolymer from the group"  
 "comprising fibrinogen", " gelatin modified by SH groups", "  
 "\*\*collagen\*\*"  
 "modified by SH groups", " or regenerated oxycellulose modified by SH groups."  
 "Said collagenous dressing is tissue-agglutinable and does not have the"  
 "disadvantages of conventional fibrin bonding in combination with"  
 "resorbable \*\*collagen\*\*."  
 " "  
 "SUMMARY: "  
 " "  
 "BSUM(1) "  
 " "  
 " \*\*Collagen\*\* has been used in surgery for some time. It can be used in"  
 "the form of sponges or fibers to. . . a large area", " the usual"  
 "collagenous dressings are inadequate. Attempts have therefore been made"  
 "to bond collagenous material", " such as \*\*collagen\*\* or gelatin", " to tissue"  
 "by the use of adhesives based on resorcinol-formaldehyde. While such"  
 "adhesives are hemostatic", " they are not. . . "  
 " "  
 "SUMMARY: "  
 " "  
 "BSUM(2) "  
 " "  
 " It is known that \*\*collagen\*\* in the body is crosslinked with"  
 "constituents of connective tissue. In the process", "  
 "\*\*collagen\*\* is"  
 "crosslinked through Schiff bases and aldol condensation. It is further"  
 "known that in basal membranes tissue strength is enhanced through"  
 "disulfide bridges of the basal membrane \*\*collagen\*\*. It is also known to"  
 "crosslink proteins such as albumin with intermolecular disulfide bonds"  
 "through disulfide bridges after mild reduction. . . network during the"  
 "end phase of the plasmatic coagulation. It is also known that individual"  
 "fibrin molecules are crosslinked through \*\*transglutaminase\*\*.  
 In the"  
 "process", " new peptide bonds are formed between glutamic acid and lysine"  
 "respectively located on adjacent chains. Through the. . . "

" "

"SUMMARY: "

" "

"BSUM(3) "

" "

" The . . . (ie. adhere to) the tissue and which does not have the  
 "known drawbacks of fibrin bonding in combination with  
 resorbable"  
 "\*\*collagen\*\*". Coupled with this object is an improvement to  
 collagenous"  
 "dressings for local hemostasis."  
 " "

"SUMMARY: "

" "

"BSUM(4) "

" "

" This object is accomplished through a tissue-adherent  
 collagenous"  
 "dressing which is characterized in that it contains \*\*collagen\*\*  
 in"  
 "combination with a resorbable biopolymer from the group  
 comprising"  
 "fibrinogen", "gelatin modified to contain SH groups", "  
 \*\*collagen\*\* modified"  
 "to contain SH groups", "or oxycellulose modified to contain SH  
 groups."  
 " "

"SUMMARY: "

" "

"BSUM(5) "

" "

" \*\*Collagen\*\* and fibrinogen or the gelatin modified by SH  
 groups", "  
 "similarly modified \*\*collagen\*\* or similarly modified  
 oxycellulose may"  
 "advantageously be combined with each other through freeze  
 drying."  
 "However", "in the case of a combination of \*\*collagen\*\* and  
 \*\*collagen\*\*"  
 "modified to contain SH groups it is also possible to introduce  
 SH groups"  
 "into the \*\*collagen\*\*."  
 " "

"SUMMARY: "

" "

"BSUM(6) "

" "

" The invention will now be described with reference to a  
 combination of"  
 "\*\*collagen\*\* and fibrinogen; however", "fibrinogen here takes  
 the place of"  
 "said resorbable biopolymers", "namely", "gelatin modified to  
 contain SH"

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"=> s lysyl oxidase"
"      1181 LYSYL"
"      5773 OXIDASE"
"L1      51 LYSYL OXIDASE"
"      (LYSYL(W) OXIDASE) "
"=> s transglutaminase"
"L2      107 TRANSGLUTAMINASE"
"=> s l1 and l2"
"L3      1 L1 AND L2"
"=> d l3"
" "
"1.  5",486,599," Jan. 23"," 1996"," Construction and use of
synthetic"
"constructs encoding syndecan; Scott Saunders"," et al. ","
530/395; 435/69.1",""
"69.7"," 252.3"," 320.1; 536/23.4"," 23.5; 935/10"," 47"," 50","
70 [IMAGE AVAILABLE]"
"=> d l3 kwic"
" "
"US PAT NO:      5",486,"599 [IMAGE AVAILABLE]                L3: 1
of 1"
" "
"DETDISC: "
" "
"DETD(41) "
" "
" This . . . the predicted mature protein is located in the
putative"
"transmembrane domain. It also does not appear to be cross-linked
by"
"***lysyl** **oxidase**- or **transglutaminase**-mediated
reactions because"
".beta.-aminopropionitrile and monodansylcadaverine treatments
of NMuMG"
"cells do not change its mobility on SDS-PAGE. Proteins with
regions rich."
" "
"=> s collagen iii"
"      8200 COLLAGEN"
"      305454 III"
"L4      12 COLLAGEN III"
"      (COLLAGEN(W) III) "
"=> d l4 1-12"
" "
"1.  5",478,739," Dec. 26"," 1995"," Three-dimensional stromal
cell and tissue"
"culture system; Sandra R. Slivka"," et al. "," 435/240.23","
240.2"," 240.241",""
"240.243; 623/15 [IMAGE AVAILABLE]"
" "
"2.  5",421,337," Jun. 6"," 1995"," Spectral diagnosis of
diseased tissue;"
"Rebecca Richards-Kortum"," et al. "," 128/665 [IMAGE AVAILABLE]"
" "

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"3. 5",416,074," May 16"," 1995"," Artificial biological membrane; Michel  
"Rabaud"," et al.", " 514/21; 530/353", " 356 [IMAGE AVAILABLE] "  
" "

"4. 5",201,745," Apr. 13"," 1993"," Visceral surgery patch; Jean-Louis Tayot", "  
"et al.", " 606/151; 424/428", " 444; 600/37; 602/50; 623/11", " 66  
[IMAGE"  
"AVAILABLE] "  
" "

"5. 5",112,757," May 12"," 1992"," Method for obtaining human hepatocyte"  
"cultures; Christiane Guguen-Guillouzo", " et al.", " 435/240.2", " 240.21 [IMAGE"  
"AVAILABLE] "  
" "

"6. 5",096,593," Mar. 17"," 1992"," Separation material derived from"  
"glucomannan for blood coagulation factor", " preparation and use thereof; "  
"Masaaki Wakita", " et al.", " 210/656", " 198.2", " 502.1; 436/513", " 529; 502/402", "  
"404; 530/381", " 383", " 413 [IMAGE AVAILABLE] "  
" "

"7. 5",089,422," Feb. 18"," 1992"," Vitro bleeding time determination; Daniel"  
"B. Brubaker", " 436/69; 73/64.41; 422/58", " 73; 436/165", " 809  
[IMAGE AVAILABLE] "  
" "

"8. 4",971,964," Nov. 20"," 1990"," Pyridine derivatives; Koji Suzuki", " et al.", "  
"514/215", " 278", " 290; 540/221", " 543", " 577; 546/17", " 65", " 93  
[IMAGE AVAILABLE] "  
" "

"9. 4",939,088," Jul. 3"," 1990"," Sustained production of recombinant gamma"  
"interferon using an Epstein-Barr virus replicon; Janet M. Young", " et al.", "  
"435/69.51; 424/85.5; 435/240.2", " 240.26", " 320.1 [IMAGE  
AVAILABLE] "  
" "

"10. 4",897,444," Jan. 30"," 1990"," Immobilized fluorogenic substrates for"  
"enzymes; and processes for their preparation; Paul J. Brynes", " et al.", "  
"525/54.1; 435/23", " 24; 530/300", " 330", " 331 [IMAGE AVAILABLE] "  
" "

"11. 4",711,783," Dec. 8"," 1987"," Forms of microencapsulation of medicinal"  
"substances by homogeneous layers of native collagen; Alain Huc", " et al.", "  
"424/460; 106/155", " 161; 424/477", " 491", " 499; 514/773", " 774", " 801; 530/356"  
"[IMAGE AVAILABLE] "

" "

"12. 4",474,761," Oct. 2"," 1984"," Oligopeptides with specific inhibiting"

"properties of collagen induced aggregation"," process for preparing the"

"same and pharmaceutical compositions containing them; Jacques Caen"," et"

"al.," 514/15"," 16"," 822; 530/328; 930/20"," DIG.802 [IMAGE AVAILABLE]"

"=> s 13 and 14"

"L5 0 L3 AND L4"

"=> s 12 and 14"

"L6 0 L2 AND L4"

"=> logoff y"

"U.S. Patent & Trademark Office LOGOFF AT 13:17:33 ON 15 MAY 96"

08/307621

lysyl oxidase ≠

transglutaminase

"=> s transglutaminase or glutaminase"

" 107 TRANSGLUTAMINASE"

" 90 GLUTAMINASE"

"L1 195 TRANSGLUTAMINASE OR GLUTAMINASE"

"=> s scar or mark or bruise"

" 3075 SCAR"

" 70701 MARK"

" 460 BRUISE"

"L2 74010 SCAR OR MARK OR BRUISE"

"=> s l1 and l2"

"L3 14 L1 AND L2"

"=> d l3 1-14"

" "

"1. 5",514,565," May 7"," 1996"," Enzymatically-produced dimeric IL-2 and a"

"nerve-derived \*\*transglutaminase\*\* enzyme for its preparation; Michael"

"Schwartz"," et al.", " 435/68.1 [IMAGE AVAILABLE]"

" "

"2. 5",468,617," Nov. 21"," 1995"," Steroid/thyroid hormone receptor-related"

"gene"," which is inappropriately expressed in human hepatocellular"

"carcinoma"," and which is a retinoic acid receptor; Hughes Blaudin De The"," "

"et al.", " 435/7.8"," 7.1; 436/63"," 501; 530/350 [IMAGE AVAILABLE]"

" "

"3. 5",455,158," Oct. 3"," 1995"," Fibrin binding domain polypeptides and uses"

"and methods of producing same; Tikva Vogel"," et al.", " 435/7.21; 424/1.69"," "

"9.341"," 9.4; 435/7.8"," 13; 436/69"," 503"," 504 [IMAGE AVAILABLE]"

" "

"4. 5",378,455," Jan. 3"," 1995"," Cosmetic composition for inhibiting hair"

"growth; George T. E. Kealey"," et al.", " 424/73"," 62"," 70.1"," 70.6"," 401 [IMAGE"

"AVAILABLE]"

" "

"5. 5",376,530," Dec. 27"," 1994"," Steroid/thyroid hormone receptor-related"

"gene"," which is inappropriately expressed in human hepatocellular"

"carcinoma"," and which is a retinoic acid receptor; Hughes B. De The"," et"

"al.", " 435/6"," 69.1"," 172.3; 530/326"," 327"," 350"," 828; 536/23.1"," 24.31 [IMAGE"

"AVAILABLE]"

" "

"6. 5",317,090," May 31"," 1994"," Steroid/thyroid hormone receptor-related"

"gene"," which is inappropriately expressed in human

hepatocellular"

"carcinoma", " and which is a retinoic acid receptor; Hughes  
Blaudin De The", ""

"et al.", " 530/387.1", " 387.9", " 388.1", " 388.22", " 391.1 [IMAGE  
AVAILABLE] "

" "

"7. 5", 270,030, " Dec. 14", " 1993", " Fibrin binding domain  
polypeptide and"

"method of producing; Tikva Vogel", " et al.", " 424/1.69", "  
9.341", " 9.4; 435/69.1", ""

"240.1", " 252.3", " 252.33", " 320.1; 530/350", " 395 [IMAGE  
AVAILABLE] "

" "

"8. 5", 151,412, " Sep. 29", " 1992", " Pharmaceutically active  
conjugates having"

"improved body tissue binding specificity; Robert A. Brown", "  
514/8; "

"435/177; 514/2", " 6", " 21; 530/363", " 380", " 382", " 391.9", "  
395", " 400", " 402 [IMAGE"

"AVAILABLE] "

" "

"9. 4", 762,707, " Aug. 9", " 1988", " New conjugates associating", "  
by covalent"

"bond", " an enzyme with an antibody", " and medicinal associations  
using the"

"said conjugates; Franz Jansen", " et al.", " 424/180.1", " 94.3  
[IMAGE AVAILABLE] "

" "

"10. 4", 701,446, " Oct. 20", " 1987", " Pyrethroid containing  
pharmaceutical"

"compositions; Jose A. Arias", " 514/65; 424/711; 514/762", " 895  
[IMAGE"

"AVAILABLE] "

" "

"11. 4", 675,313, " Jun. 23", " 1987", " Pyrethroid-containing  
pharmaceutical"

"compositions; Jose A. Arias", " 514/65", " 762", " 894", " 934  
[IMAGE AVAILABLE] "

" "

"12. 4", 623,626, " Nov. 18", " 1986", " L-glutamic acid oxidase and  
its"

"production; Hitoshi Kusakabe", " et al.", " 435/191", " 886 [IMAGE  
AVAILABLE] "

" "

"13. 4", 614,714, " Sep. 30", " 1986", " Use of novel L-glutamic  
acid oxidase; "

"Hitoshi Kusakabe", " et al.", " 435/25", " 191", " 287.9", " 810", "  
817 [IMAGE AVAILABLE] "

" "

"14. 4", 396,628, " Aug. 2", " 1983", " Antiviral activities of  
dansylcadaverine"

"and closely related compounds; Ira H. Pastan", " et al.", "  
514/603 [IMAGE"

"AVAILABLE] "

"=> d 13 12 kwic"

" "

"US PAT NO: 4",623,"626 [IMAGE AVAILABLE]  
of 14"

L3: 12

" "

"SUMMARY: "

" "

"BSUM(22) "

" "

" The . . . screening of glutamic acid producing  
microorganisms. Also",""

"since activity assays of enzymes forming glutamic acid as the  
product"

"such as \*\*glutaminase\*\*"," glutamic acid-oxaloacetic acid  
transaminase"

"(GOT)"," glutamic acid-pyruvic acid transaminase (GPT)"," and"

".gamma.-glutamyl transpeptidase (.gamma.-GTP) can easily be done  
by the."

" . . . "

" "

"DETDESC: "

" "

"DETD(38) "

" . . . . "

"

94.4"

"NiCl.sub.2"

" 96.5

NaN.sub.3

100.6"

"StCl.sub.2"

" 97.2

DDTC.sup.4

100.7"

"Li.sub.2 SO.sub.4"

" 93.8

Tiron.sup.5

100.7"

"

(trade \*\*mark\*\*)"

"ZnSO.sub.4"

" 90.3"

"

"

" .sup.1 EDTA: ethylenediaminetetraacetic acid"

" .sup.2 NEM: N--ethylmaleimide"

" .sup.3 PCMB: pchloromercuribenzoate"

" .sup.4 DDTC: . . . . "

"=> s collagen"

"L4 8200 COLLAGEN"

"=> s l1 and l4"

"L5 51 L1 AND L4"

"=> d 15 1-51"

" "

"1. 5",514,579," May 7"," 1996"," Human transglutaminases;  
Patrick J. O'Hara",""

"et al.," 435/240.2"," 69.2"," 193"," 254.3"," 320.1;

536/23.2"," 24.31 [IMAGE"

"AVAILABLE]"

" "

"2. 5",510,102," Apr. 23"," 1996"," Plasma and polymer  
containing surgical"

"hemostatic adhesives; Kent C. Cochrum"," 424/78.08; 128/DIG.22;

424/530;"  
"602/52 [IMAGE AVAILABLE] "  
" "  
"3. 5",510,077," Apr. 23"," 1996"," Method of making an  
intraluminal stent;"  
"Thomas Q. Dinh"," et al.," 264/485"," 279"," 279.1"," 314","  
316"," 320"," 330"," 488"  
"[IMAGE AVAILABLE] "  
" "  
"4. 5",504,001," Apr. 2"," 1996"," Hybrid plasminogen activator;  
Donald C."  
"Foster"," 435/219; 424/94.64; 435/226 [IMAGE AVAILABLE] "  
" "  
"5. 5",490,980," Feb. 13"," 1996"," Covalent bonding of active  
agents to skin",""  
"hair or nails; Norman K. Richardson"," et al.," 424/94.6; 514/2  
[IMAGE"  
"AVAILABLE] "  
" "  
"6. 5",487,889," Jan. 30"," 1996"," Bandage for continuous  
application of"  
"biologicals; Richard L. Eckert"," et al.," 424/93.1"," 93.2","  
93.21"," 93.7;"  
"514/2"," 12; 604/304"," 305"," 307 [IMAGE AVAILABLE] "  
" "  
"7. 5",486,599," Jan. 23"," 1996"," Construction and use of  
synthetic"  
"constructs encoding syndecan; Scott Saunders"," et al.,"  
530/395; 435/69.1",""  
"69.7"," 252.3"," 320.1; 536/23.4"," 23.5; 935/10"," 47"," 50","  
70 [IMAGE AVAILABLE] "  
" "  
"8. 5",475,113," Dec. 12"," 1995"," Tetrahydronaphthyl and  
thiazole"," oxazole or"  
"imidazole substituted ethene derivatives having retinoid-like  
activity",""  
"reduced skin toxicity and reduced teratogenicity; Roshantha A."  
"Chandraratna"," 548/203"," 200"," 204"," 205"," 214"," 235","  
236"," 333.5"," 334.5 [IMAGE"  
"AVAILABLE] "  
" "  
"9. 5",455,265," Oct. 3"," 1995"," Method of treatment with  
compounds having"  
"selective agonist-like activity on RXR retinoid receptors;  
Roshantha A."  
"S. Chandraratna"," 514/448"," 438"," 444"," 452"," 461"," 467","  
471"," 510"," 531"," 546",""  
569," 617"," 684"," 700"," 717"," 719"," 729"," 765; 549/60","  
70"," 71"," 72"," 73"," 74"," 75",""  
77," 78"," 79"," 80"," 369"," 370"," 430"," 448"," 468"," 483","  
486"," 487"," 493"," 495"," 496",""  
497," 498"," 499"," 501"," 504"," 505"," 506; 560/8"," 100;  
562/405"," 490; 564/180;"  
"568/327"," 328"," 440"," 592"," 659"," 808; 585/20"," 21 [IMAGE

so A

AVAILABLE] "

" "

"10. 5",455,158," Oct. 3"," 1995"," Fibrin binding domain polypeptides and uses"

"and methods of producing same; Tikva Vogel"," et al.", " 435/7.21; 424/1.69", ""

"9.341", " 9.4; 435/7.8", " 13; 436/69", " 503", " 504 [IMAGE AVAILABLE] "

" "

"11. 5",428,014," Jun. 27"," 1995"," \*\*Transglutaminase\*\* cross-linkable" ✓

"polypeptides and methods relating thereto; Virender Labroo"," et al.", ""

"514/12", " 13", " 14", " 15", " 16; 530/324", " 326", " 327", " 328", " 329", " 345", " 350 [IMAGE"

"AVAILABLE] "

" "

"12. 5",409,731," Apr. 25"," 1995"," Method for imparting a hydrophilic nature"

"to a contact lens; Akira Nakagawa"," et al.", " 427/2.12", " 164", " 338", " 340", " 393.5"

" [IMAGE AVAILABLE] "

" "

"13. 5",368,858," Nov. 29"," 1994"," Methods and compositions for the treatment" ✓

"and repair of defects or lesions in cartilage; Ernst B. Hunziker", ""

"424/423", " 424", " 425", " 426", " 450", " 484", " 489", " 499; 514/944", " 953", " 965 [IMAGE"

"AVAILABLE] "

" "

"14. 5",366,958," Nov. 22"," 1994"," Localized delivery using fibronectin"

"conjugates; Alan L. Weiner"," et al.", " 514/2; 424/450; 530/380", " 810", " 812"

" [IMAGE AVAILABLE] "

" "

"15. 5",352,771," Oct. 4"," 1994"," Hydrolysis of peptide bonds using Pt (II)"

"and Pd (II) complexes; Nenad M. Kostic"," et al.", " 530/345", " 343 [IMAGE"

"AVAILABLE] "

" "

"16. 5",324,840," Jun. 28"," 1994"," Method of treatment with compounds having" } ✓

"retinoid-like activity and reduced skin toxicity and lacking teratogenic"

"effects; Roshantha A. S. Chandraratna", " 546/318", " 326", " 335", " 342; 549/77", ""

79, " 484", " 487", " 496", " 499 [IMAGE AVAILABLE] "

" "

"17. 5",312,751," May 17"," 1994"," Hybridoma producing a monoclonal antibody"

"specific for an antigen of the stratum corneum of human

epidermis; Serge"

"Michel", " et al.", " 435/240.27", " 70.21", " 172.2; 530/388.2  
[IMAGE AVAILABLE] "

" "

"18. 5", 292,668, " Mar. 8", " 1994", " Bispecific antibody  
determinants; Henry P."

"Paulus", " 436/547; 435/18", " 25", " 240.27; 436/548", " 819;  
530/344", " 387.3", " 390.5", ""

"408 [IMAGE AVAILABLE] "

" "

"19. 5", 271,961, " Dec. 21", " 1993", " Method for producing  
protein microspheres; "

"Edith Mathiowitz", " et al.", " 427/213.31; 424/491", " 499;  
426/96; 427/213.3", ""

"213.36 [IMAGE AVAILABLE] "

" "

"20. 5", 270,300, " Dec. 14", " 1993", " Methods and compositions  
for the treatment"

"and repair of defects or lesions in cartilage or bone; Ernst B.  
Hunziker", ""

"514/12; 424/422", " 423", " 424", " 425", " 426", " 450", " 484", "  
489", " 499; 514/2", " 8", " 56", ""

944, " 965; 530/350", " 351", " 353", " 354", " 356", " 840 [IMAGE  
AVAILABLE] "

" "

"21. 5", 270,030, " Dec. 14", " 1993", " Fibrin binding domain  
polypeptide and"

"method of producing; Tikva Vogel", " et al.", " 424/1.69", "  
9.341", " 9.4; 435/69.1", ""

"240.1", " 252.3", " 252.33", " 320.1; 530/350", " 395 [IMAGE  
AVAILABLE] "

" "

"22. 5", 206,023, " Apr. 27", " 1993", " Method and compositions for  
the treatment"

"and repair of defects or lesions in cartilage; Ernst B.  
Hunziker", ""

"424/423", " 422", " 424", " 425", " 426", " 450", " 484", " 489", " 499;  
514/2", " 8", " 944", " 953", " 965; "

"530/350", " 351", " 353", " 354", " 356", " 840 [IMAGE AVAILABLE] "

" "

"23. 5", 204,447, " Apr. 20", " 1993", " Purification of factor  
XIII; Paul D."

"Bishop", " et al.", " 530/381", " 380", " 416", " 417", " 418", "  
419", " 420", " 421 [IMAGE"

"AVAILABLE] "

" "

"24. 5", 177,092, " Jan. 5", " 1993", " Medicinal use of certain  
tetrazolium salts; "

"David C. Remy", " et al.", " 514/381; 548/251 [IMAGE AVAILABLE] "

" "

"25. 5", 158,976, " Oct. 27", " 1992", " Controlling  
glutamine/glutamate related"

"neuronal injury; Paul A. Rosenberg", " 514/561 [IMAGE AVAILABLE] "

" "



✓

"26. 5",156,956," Oct. 20"," 1992"," Transgultaminase; Masao Motoki"," et al.", ""  
"435/68.1; 426/573; 435/193 [IMAGE AVAILABLE] "  
" "

"27. 5",152,988," Oct. 6"," 1992"," Imidazole compounds in compositions and"  
"methods in thrombolytic therapy; David A. Claremon"," et al.", ""  
424/94.64;"  
"514/2"," 14"," 161"," 213"," 228.2"," 255"," 257 [IMAGE AVAILABLE] "  
" "

"28. 5",151,412," Sep. 29"," 1992"," Pharmaceutically active conjugates having"  
"improved body tissue binding specificity; Robert A. Brown"," 514/8;"  
"435/177; 514/2"," 6"," 21; 530/363"," 380"," 382"," 391.9"," 395"," 400"," 402 [IMAGE AVAILABLE] "  
" "

"29. 5",135,956," Aug. 4"," 1992"," Method of using cytoprotective alcohols to"  
"treat neural disease and neural injury; Jacques Borg"," et al.", "" 514/724"," ""  
739," 879 [IMAGE AVAILABLE] "  
" "

"30. 5",098,733," Mar. 24"," 1992"," Novel gel-like food articles and process"  
"for producing the same; Nobuo Kyogoku"," et al.", "" 426/573"," 104"," 574"," 656;"  
"530/378"," 408 [IMAGE AVAILABLE] "  
" "

"31. 5",098,707," Mar. 24"," 1992"," Imidazole compounds and their use as"  
"\*\*\*transglutaminase\*\* inhibitors; John J. Baldwin"," et al.", "" 424/94.64;"  
"514/2"," 56"," 161"," 258"," 398"," 822 [IMAGE AVAILABLE] "  
" "

"32. 5",093,028," Mar. 3"," 1992"," Gelled emulsion and process for producing"  
"the same; Nobuo Kyogoku"," et al.", "" 252/315.1"," 312; 426/573 [IMAGE AVAILABLE] "  
" "

"33. 5",084,444," Jan. 28"," 1992"," Imidazole compounds and their use as"  
"\*\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.", "" 514/15"," 16"," ""  
18," 393; 530/328"," 329"," 331 [IMAGE AVAILABLE] "  
" "

"34. 5",077,285," Dec. 31"," 1991"," Imidazole compounds and their use as"  
"\*\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.", "" 514/15"," 16"," ""  
"18; 530/328"," 329"," 331 [IMAGE AVAILABLE] "

" "

"35. 5",047,416," Sep. 10"," 1991"," Triazole compounds and their use as"  
 "\*\*\*transglutaminase\*\* inhibitors; David C. Remy"," et al.", " 514/384; 546/119;"  
 "548/251"," 255"," 264.4"," 370.4 [IMAGE AVAILABLE]"  
 " "

"36. 5",037,664," Aug. 6"," 1991"," Process for producing novel gel-like food"  
 "articles; Nobuo Kyogoku"," et al.", " 426/573"," 656; 530/408 [IMAGE AVAILABLE]"  
 " "

"37. 5",030,644," Jul. 9"," 1991"," Imidazole compounds and their use as"  
 "\*\*\*transglutaminase\*\* inhibitors; John J. Baldwin"," et al.", " 514/393"," 252"," "  
 "253"," 256"," 278"," 338"," 341"," 395"," 398; 544/333"," 406; 546/15"," 271"," 278;"  
 "548/302.7"," 307.1"," 321.5"," 324.1 [IMAGE AVAILABLE]"  
 " "

"38. 5",021,440," Jun. 4"," 1991"," Imidazole compounds and their use as"  
 "\*\*\*transglutaminase\*\* inhibitors; David C. Remy"," et al.", " 514/381"," 393"," "  
 "397; 548/251"," 302.7"," 312.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"  
 " "

"39. 5",019,572," May 28"," 1991"," Imidazole compounds and their use as"  
 "\*\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.", " 514/213"," "  
 "228.2"," 255"," 326"," 398; 540/451; 544/61"," 359; 546/210; 548/302.7"," 314.7"," "  
 "315.1"," 315.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"  
 " "

"40. 4",968,713," Nov. 6"," 1990"," Certain imidazole compounds as"  
 "\*\*\*transglutaminase\*\* inhibitors; John J. Baldwin"," et al.", " 514/398;"  
 "548/324.1 [IMAGE AVAILABLE]"  
 " "

"41. 4",708,861," Nov. 24"," 1987"," Liposome-gel compositions; Mircea C."  
 "Popescu"," et al.", " 424/1.21; 264/4.1"," 4.32; 424/1.25"," 450"," 457"," 458"," 460"," "  
 "462"," 484; 428/402.2 [IMAGE AVAILABLE]"  
 " "

"42. 4",614,714," Sep. 30"," 1986"," Use of novel L-glutamic acid oxidase;"  
 "Hitoshi Kusakabe"," et al.", " 435/25"," 191"," 287.9"," 810"," 817 [IMAGE AVAILABLE]"  
 " "

"43. 4",532,123," Jul. 30"," 1985"," Dual Microcapsules and process for their"

"preparation; David L. Gardner", " 424/497; 71/DIG.1; 264/4.1", " 4.3; 424/94.3", ""  
"DIG.7; 428/402.2", " 402.21 [IMAGE AVAILABLE] "  
" "  
"44. 4",472,498," Sep. 18", " 1984", " Analysis film and a method of analysis"  
"using the same; Nobuhito Masuda", " et al.", " 435/7.7; 422/56", " 57; 435/7.71", ""  
"7.72", " 7.9", " 805", " 970; 436/500", " 527", " 537", " 810", " 815 [IMAGE AVAILABLE] "  
" "  
"45. 4",444,878," Apr. 24", " 1984", " Bispecific antibody determinants; Henry P."  
"Paulus", " 435/7.1; 204/403; 422/55; 435/7.5", " 7.91", " 18", " 25", " 28", " 175", " 177", ""  
"179", " 188", " 287.2", " 287.9", " 805", " 810", " 817", " 962", " 964", " 966", " 969; 436/512", " 518", ""  
"528", " 530", " 548", " 808 [IMAGE AVAILABLE] "  
" "  
"46. 4",407,787," Oct. 4", " 1983", " Collagenous dressing; Axel Stemberger", ""  
"424/444; 106/122", " 125", " 128", " 161; 514/21", " 57", " 801", " 802; 530/356", " 381; "  
"602/49", " 50; 604/304 [IMAGE AVAILABLE] "  
" "  
"47. 4",325,867," Apr. 20", " 1982", " Process for the recovery of"  
".alpha.-2-SB-glycoprotein; Walter Eberle", " et al.", " 530/392", " 353", " 354", " 356", ""  
"381", " 395", " 411", " 413", " 830 [IMAGE AVAILABLE] "  
" "  
"48. 4",307,195," Dec. 22", " 1981", " Immobilized enzyme membrane; Yoshiharu"  
"Karasawa", " et al.", " 435/287.9; 204/403; 435/179", " 181", " 182 [IMAGE AVAILABLE] "  
" "  
"49. 4",061,141," Dec. 6", " 1977", " Apparatus and method for selectively"  
"separating amino acids and defined proteins in blood; Viktor Holger"  
"Hyden", " et al.", " 604/5; 128/DIG.3; 422/44; 435/14", " 177", " 179", " 181", " 182", ""  
"293.1", " 297.2", " 299.1 [IMAGE AVAILABLE] "  
" "  
"50. 3",849,254," Nov. 19", " 1974", " PROCESS FOR EFFECTING ENZYMATIC REACTIONS"  
"IN AEROSOLS; Donald J. Kirwan", " et al.", " 435/176", " 179", " 180", " 199", " 213", " 236", ""  
"822", " 882", " 885 [IMAGE AVAILABLE] "  
" "  
"51. 3",839,175," Oct. 1", " 1974", " ELECTRODEPOSITION OF ENZYMES; Melvin H."  
"Keyes", " 435/176; 204/489; 435/283.1", " 287.9", " 817 [IMAGE AVAILABLE] "

"=> d 15 26 kwic"

" "

"US PAT NO: 5",156,"956 [IMAGE AVAILABLE]  
of 51"

L5: 26

" "

"ABSTRACT: "

"A \*\*transglutaminase\*\* catalyzing an acyl transfer reaction of  
a"

".gamma.-carboxyamide group of a glutamine residue in a peptide  
or protein"

"chain in. . . "

" "

"SUMMARY: "

" "

"BSUM(3) "

" "

" The present invention relates to a novel \*\*transglutaminase\*\*  
and a"

"process for producing a protein gelation product using the"

"\*\*transglutaminase\*\*."

" "

"SUMMARY: "

" "

"BSUM(9) "

" "

" Up to now", " however", " no report has been made on any  
\*\*transglutaminase\*\*"

"derived from microorganisms. With respect to a process for  
producing gel"

"products of protein using an animal-derived

\*\*transglutaminase\*\*", " the"

"present inventors have already made investigations resulting in  
Published"

"Unexamined Japanese Patent Application No. 149645/83."

" "

"SUMMARY: "

" "

"BSUM(10) "

" "

" However", " application of the animal-derived

\*\*transglutaminase\*\* to"

"industry", " particularly", " the process for producing protein  
gelation"

"products involves defects as described below."

" "

"SUMMARY: "

" "

"BSUM(11) "

" "

" It . . . substrate protein and at least 2.0 wt. % of a  
substrate"

"protein concentration are required for gelation. Further", " the"

"animal-derived \*\*transglutaminase\*\* is calcium

(Ca.sup.2+) dependent so"

"that its application is limited."

" "

"DRAWING DESC: "

" "

"DRWD(8) "

" "

" Accordingly", " an object of the present invention is to provide a new"

"\*\*transglutaminase\*\* which is free from problems such as quantity of"

"supply", " cost/performance", " and ease of purification."

" "

"DRAWING DESC: "

" "

"DRWD(9) "

" "

" It is another object of the present invention to provide a"

"\*\*transglutaminase\*\* which has great practicality since no calcium is"

"required for the reaction catalyzed by the

"\*\*transglutaminase\*\*."

" "

"DRAWING DESC: "

" "

"DRWD(10) "

" "

" The present invention is further directed to a method for producing a"

"protein gelation product by using a \*\*transglutaminase\*\*."

" "

"DRAWING DESC: "

" "

"DRWD(11) "

" "

" The above and other objects which will become more readily apparent"

"hereinafter", " have been achieved by the discovery of a novel"

"\*\*transglutaminase\*\* derived from microorganisms."

" "

"DRAWING DESC: "

" "

"DRWD(13) "

" "

" Animal-derived . . . been investigated heretofore but due to lack of"

"practicability", " the present inventors have made wide-ranging"

"investigations", " searching for a microorganism-derived"

"\*\*transglutaminase\*\*. As a result", " it has been found that bacteria"

"belonging to the genus Streptoverticillium are capable of producing novel"

"transglutaminases. . . . "

" "

"DRAWING DESC: "

" "

"DRWD(15) "

" "

" Methods for culture", " purification", " etc.", " which comprise culturing these"

"microorganisms and harvesting \*\*transglutaminase\*\* (hereafter referred to"

"as BTGase) will be described below. For the purposes of the present"

"invention", " any culturing mode of. . . "

" "

"DRAWING DESC: "

" "

"DRWD(28) "

" "

" Enzymological properties of the thus obtained purified BTGases", " namely", "

"\*\*transglutaminase\*\* of Streptoverticillium mobaraense IFO 13819 (named"

"BTG-1)", " \*\*transglutaminase\*\* of Streptoverticillium griseocarneum IFO"

"12776 (named BTG-2) and \*\*transglutaminase\*\* of Streptoverticillium"

"cinnamoneum sub sp. cinnamoneum IFO 12852 (named BTG-3) are described"

"below."

" "

"DRAWING DESC: "

" "

"DRWD(51) "

" "

" Next", " properties of BTGases are compared to those of guinea pig"

"liver-derived \*\*transglutaminase\*\*. The guinea pig liver-derived"

"\*\*transglutaminase\*\* was prepared by the method described in Published"

"Unexamined Japanese Patent Application No. 149645/83. In Table 4", ""

"comparison in enzymological. . . in Table 5. As will be apparent from"

"Tables 4 and 5", " various differences in enzymological properties are noted"

"between \*\*transglutaminase\*\* of guinea pig liver (hereafter referred to"

"as MTGase) which has been mainly investigated heretofore and BTGases"

"derived from actinomycetes;. . . "

" "

"DRAWING DESC: "

" "

"DRWD(55) "

" "

" First", " . . . therefrom. The kind of animal protein is not"

"particularly limited but there may be mentioned", " for example", " milk"

"protein", " gelatin", " \*\*collagen\*\*", " serum albumin", " etc."

" "

"DETDESC: "

" "

"DETD(4) "

" "

" The . . . by Rohm & Haas Co.", " Ltd.)", " which had been previously"

"equilibrated with 0.05M phosphate buffer (pH 6.5). By this operation", ""

"\*\*transglutaminase\*\* was adsorbed. After washing protein impurities out"

"with the buffer", " a density gradient of 0.05 to 0.5M was prepared by. ."

". have a conductivity of 10 ms or less", " it was passed through a column"

"of blue Sepharose. By this operation", " \*\*transglutaminase\*\* was adsorbed."

"After washing protein impurities out with 0.05M phosphate buffer (pH 7)", ""

"a density gradient of 0 to 1M. . . "

" "

"DETDESC: "

" "

"DETD(63) "

" "

" A necessary amount of oxhide-derived atelo-\*\*collagen\*\* powders"

"(manufactured by Kouken K.K.) were taken in a test tube and 2 ml of 0.1M"

"Tris-HCl buffer (pH 7.5). . . maintaining in a water bath at"

"55.degree. C. for 15 minutes", " the mixture was stirred to prepare 3 to 10%"

"atelo-\*\*collagen\*\* solutions. Before the solutions of high concentration"

"were gelled due to cooling", " BTGase was added thereto in 0.05 U/mg protein"

"followed by incubation at 55.degree. C. for 60 minutes. As a control for"

"the all samples", " 10% atelo-\*\*collagen\*\* solution with no BTGase added was"

"also incubated likewise. Immediately after completion of the incubation", ""

"the system was allowed to. . . "

" "

"CLAIMS: "

" "

"CLMS(1) "

" "

" What is claimed as new and desired to be secured by Letters Patent of"

"the United States:"

" "

" 1. A **\*\*transglutaminase\*\*** which catalyzes an acyl transfer reaction of a"  
".gamma.-carboxyamide group of a glutamine residue in a peptide or protein"  
"chain. . . . "  
" "

"CLAIMS: "  
" "

"CLMS(2) "  
" "

" 2. The **\*\*transglutaminase\*\*** of claim 1"," obtained from a microorganism of"  
"the genus Streptovercillium."  
" "

"CLAIMS: "  
" "

"CLMS(3) "  
" "

" 3. A process for producing a **\*\*transglutaminase\*\***"," which comprises"  
"culturing a microorganism of a strain belonging to the genus"  
"Streptovercillium capable of producing a **\*\*transglutaminase\*\*** which"  
"catalyzes an acyl transfer reaction of a .gamma.-carboxyamide group of a"  
"glutamine residue in a peptide or protein chain independently of"  
"Ca.sup.2+"," and harvesting said **\*\*transglutaminase\*\*** from the culture."  
" "

"CLAIMS: "  
" "

"CLMS(4) "  
" "

" 4. . . . which comprises contacting a protein-containing solution or"  
"slurry having a protein concentration of at least 1.0 wt. % with a"  
"**\*\*transglutaminase\*\*** which catalyzes an acyl transfer reaction of a"  
".gamma.-carboxyamide group of a glutamine residue in a peptide or protein"  
"chain. . . . "  
" "

"CLAIMS: "  
" "

"CLMS(5) "  
" "

" 5. A process as claimed in claim 4 wherein 0.01 to 2000 units of said"  
"**\*\*transglutaminase\*\*** are incorporated per 1.0 g of the protein contained"  
"in said solution or slurry."



" "

"CLAIMS: "

" "

"CLMS(6) "

" "

" 6. The process of claim 4", " wherein said \*\*transglutaminase\*\* is obtained"

"from the genus Streptoverticillium."

"=> d 15 37 kwic"

" "

"US PAT NO: 5",030,"644 [IMAGE AVAILABLE]  
of 51"

L5: 37

"TITLE: Imidazole compounds and their use as

\*\*transglutaminase\*\*"

" inhibitors"

" "

"ABSTRACT: "

"Imidazole compounds including imidazoles and imidazolium salts", " and their"

"use as \*\*transglutaminase\*\* inhibitors are disclosed."

" "

"SUMMARY: "

" "

"BSUM(3) "

" "

" A number of disease states have been associated with"  
\*\*transglutaminase\*\* activity Thus", " for example", " in acne lesions", ""

\*\*transglutaminase\*\* activity in sebaceous follicles has been reported by"

"DeYoung et. al.", " in J. Investigative Dermatology", " 82", " 275 (1984). Also", ""

"the cornified cell envelope in acne has been reported to be a result of"

\*\*transglutaminase\*\* activity by Dalziel et. al.", " Br. J. Exp. Pathology", ""

" "

"SUMMARY: "

" "

"BSUM(4) "

" "

" Another dermatological disease", " psoriasis", " is reported to be associated"

"with excessive \*\*transglutaminase\*\* activity by Bernard et. al. British"

"Journal of Dermatology", " 114", " 279 (1986) "

" "

"SUMMARY: "

" "

"BSUM(5) "

" "

" Cataracts also have been reported to be associated with elevated"

\*\*transglutaminase\*\* activities."

" "

"SUMMARY: "

" "

"BSUM(6) "

" "

" Factor XIIIa is a plasma \*\*transglutaminase\*\* which is the activated"

"form of Factor XIII also known as fibrinase or fibrin stabilizing factor."

"It is essential for. . . "

" "

"SUMMARY: "

" "

"BSUM(11) "

" "

" A novel class of imidazole compounds has been discovered which inhibits"

"\*\*transglutaminase\*\* activity", " particularly Factor XIIIa activity. The"

"invention also embraces composition and methods for using the imidazole"

"compounds as Factor XIIIa. . . . "

" "

"DETDESC: "

" "

"DETD(43) "

" "

" The compounds of the present invention are useful as"

"\*\*transglutaminase\*\* inhibitors", " particularly as Factor XIIIa inhibitors", ""

"and are adapted to be employed in thrombolytic therapy. In such use", " it"

"is. . . . "

" "

"DETDESC: "

" "

"DETD(45) "

" "

" Also", " . . . frequently Arg-Gly-Asp. Some classes of natural proteins"

"having this property are fibrinogen receptor antagonists", " thromboxane"

"receptor antagonists", " thromboxane synthesis inhibitors", " \*\*collagen\*\*"

"receptor antagonists and thrombin inhibitors. Among especially useful"

"polypeptides are those designated Echistatin and Bitistatin and" "having the amino acid. . . . "

" "

"DETDESC: "

" "

"DETD(47) "

" "

" The preferred compounds for use as \*\*transglutaminase\*\*"

inhibitors are"  
"the quaternary imidazolium salts."

" "  
"DETD(83) "

" "  
"DETD(83) "

" The preparation of the imidazole compounds suitable for inhibiting"

"\*\*transglutaminase\*\* enzymes", " particularly Factor XIIIa", " and compositions"

"suitable for carrying out the process of the present invention are"

"illustrated by the. . . "

"=> s amine or amino"

" 120602 AMINE"

" 128100 AMINO"

" "

L6 182505 AMINE OR AMINO"

"=> s 15 and 16"

"L7 47 L5 AND L6"

"=> s spermidine or putrescine"

" 776 SPERMIDINE"

" 351 PUTRESCINE"

"L8 999 SPERMIDINE OR PUTRESCINE"

"=> s 17 and 18"

"L9 20 L7 AND L8"

"=> d 19 1-20"

" "

"1. 5",490,980," Feb. 13", " 1996", " Covalent bonding of active agents to skin", ""

"hair or nails; Norman K. Richardson", " et al.", " 424/94.6; 514/2 [IMAGE"

"AVAILABLE] "

" "

"2. 5",475,113," Dec. 12", " 1995", " Tetrahydronaphthyl and thiazole", " oxazole or"

"imidazole substituted ethene derivatives having retinoid-like activity", ""

"reduced skin toxicity and reduced teratogenicity; Roshantha A."

"Chandraratna", " 548/203", " 200", " 204", " 205", " 214", " 235", "

236", " 333.5", " 334.5 [IMAGE"

"AVAILABLE] "

" "

"3. 5",455,265," Oct. 3", " 1995", " Method of treatment with compounds having"

"selective agonist-like activity on RXR retinoid receptors; Roshantha A."

"S. Chandraratna", " 514/448", " 438", " 444", " 452", " 461", " 467", " 471", " 510", " 531", " 546", ""

569, " 617", " 684", " 700", " 717", " 719", " 729", " 765; 549/60", "

70", " 71", " 72", " 73", " 74", " 75", ""

77, " 78", " 79", " 80", " 369", " 370", " 430", " 448", " 468", " 483", "

486", " 487", " 493", " 495", " 496", ""

497," 498"," 499"," 501"," 504"," 505"," 506; 560/8"," 100;  
562/405"," 490; 564/180;"  
"568/327"," 328"," 440"," 592"," 659"," 808; 585/20"," 21 [IMAGE  
AVAILABLE]"

" "

"4. 5",455,158," Oct. 3"," 1995"," Fibrin binding domain  
polypeptides and uses"

"and methods of producing same; Tikva Vogel"," et al.,"  
435/7.21; 424/1.69"," "

"9.341"," 9.4; 435/7.8"," 13; 436/69"," 503"," 504 [IMAGE  
AVAILABLE]"

" "

"5. 5",366,958," Nov. 22"," 1994"," Localized delivery using  
fibronectin"

"conjugates; Alan L. Weiner"," et al.," 514/2; 424/450;  
530/380"," 810"," 812"

"[IMAGE AVAILABLE]"

" "

"6. 5",324,840," Jun. 28"," 1994"," Method of treatment with  
compounds having"

"retinoid-like activity and reduced skin toxicity and lacking  
teratogenic"

"effects; Roshantha A. S. Chandraratna"," 546/318"," 326","  
335"," 342; 549/77"," "

79," 484"," 487"," 496"," 499 [IMAGE AVAILABLE]"

" "

"7. 5",270,030," Dec. 14"," 1993"," Fibrin binding domain  
polypeptide and"

"method of producing; Tikva Vogel"," et al.," 424/1.69","  
9.341"," 9.4; 435/69.1"," "

"240.1"," 252.3"," 252.33"," 320.1; 530/350"," 395 [IMAGE  
AVAILABLE]"

" "

"8. 5",204,447," Apr. 20"," 1993"," Purification of factor XIII;  
Paul D."

"Bishop"," et al.," 530/381"," 380"," 416"," 417"," 418","  
419"," 420"," 421 [IMAGE

"AVAILABLE]"

" "

"9. 5",177,092," Jan. 5"," 1993"," Medicinal use of certain  
tetrazolium salts;"

"David C. Remy"," et al.," 514/381; 548/251 [IMAGE AVAILABLE]"

" "

"10. 5",152,988," Oct. 6"," 1992"," Imidazole compounds in  
compositions and"

"methods in thrombolytic therapy; David A. Claremon"," et al.,"  
424/94.64;"

"514/2"," 14"," 161"," 213"," 228.2"," 255"," 257 [IMAGE  
AVAILABLE]"

" "

"11. 5",135,956," Aug. 4"," 1992"," Method of using  
cytoprotective alcohols to"

"treat neural disease and neural injury; Jacques Borg"," et  
al.," 514/724"," "

739," 879 [IMAGE AVAILABLE]"

" "

"12. 5",098,707," Mar. 24"," 1992"," Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; John J. Baldwin"," et al.",," 424/94.64;"

"514/2"," 56"," 161"," 258"," 398"," 822 [IMAGE AVAILABLE]"

" "

"13. 5",084,444," Jan. 28"," 1992"," Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.",," 514/15"," 16"," "

18," 393; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"14. 5",077,285," Dec. 31"," 1991"," Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.",," 514/15"," 16"," "

"18; 530/328"," 329"," 331 [IMAGE AVAILABLE]"

" "

"15. 5",047,416," Sep. 10"," 1991"," Triazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; David C. Remy"," et al.",," 514/384; 546/119;"

"548/251"," 255"," 264.4"," 370.4 [IMAGE AVAILABLE]"

" "

"16. 5",030,644," Jul. 9"," 1991"," Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; John J. Baldwin"," et al.",," 514/393"," 252"," "

253," 256"," 278"," 338"," 341"," 395"," 398; 544/333"," 406; 546/15"," 271"," 278;"

"548/302.7"," 307.1"," 321.5"," 324.1 [IMAGE AVAILABLE]"

" "

"17. 5",021,440," Jun. 4"," 1991"," Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; David C. Remy"," et al.",," 514/381"," 393"," "

"397; 548/251"," 302.7"," 312.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"

" "

"18. 5",019,572," May 28"," 1991"," Imidazole compounds and their use as"

"\*\*transglutaminase\*\* inhibitors; David A. Claremon"," et al.",," 514/213"," "

"228.2"," 255"," 326"," 398; 540/451; 544/61"," 359; 546/210; 548/302.7"," 314.7"," "

"315.1"," 315.7"," 324.1"," 325.1 [IMAGE AVAILABLE]"

" "

"19. 4",968,713," Nov. 6"," 1990"," Certain imidazole compounds as"

"\*\*transglutaminase\*\* inhibitors; John J. Baldwin"," et al.",," 514/398;"

"548/324.1 [IMAGE AVAILABLE]"